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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/712,494	11/13/2003	Doris Brugger	21487	8326
151 7590 06/01/2007 HOFFMANN-LA ROCHE INC. PATENT LAW DEPARTMENT 340 KINGSLAND STREET NUTLEY, NJ 07110			EXAMINER HISSONG, BRUCE D	
			ART UNIT 1646	PAPER NUMBER
			MAIL DATE 06/01/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/712,494	Applicant(s) BRUGGER ET AL.	
	Examiner Bruce D. Hissong, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) 7-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 11-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Formal Matters

1. Applicants' response to the office action mailed on 10/30/2006, including amendments to the claims and specification, was received on 3/5/2007 and have been entered into the record.

2. Claims 1-13 are currently pending. Claims 7-10 are withdrawn as non-elected subject matter, and claims 1-6 and 11-13 are the subject of this office action.

Drawings

The drawings received on 7/9/2004 remain objected to for reasons of record as set forth on the Form PTO-948 mailed on 10/30/2006. In the reply received on 3/5/2007, the Applicants state that replacement drawings are currently being prepared and will be submitted upon completion.

Specification

1. Objection to the specification regarding improper use of trademarks, as set forth on page 3 of the office action mailed on 10/30/2006, is *maintained* for reasons of record.

2. Objection to the specification regarding the description of the figures, as set forth on page 3 of the office action mailed on 10/30/2006, is *maintained*. In the response received on 3/5/2007, the Applicants have amended the specification to recite Figure 2A and 2B, and Figure 3A and 3B. However, the amendments do not describe the contents of each individual panel. It is also noted that Figures 5 and 6 also contain multiple panels that have not been described in the specification, and that there are two figures labeled as "Figure 8".

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Claim Objections

The objections to claims 1, 6, and 11, regarding minor informalities in the claims, as set forth on page 3 of the office action mailed on 10/30/2006, are withdrawn in response to Applicants' amendments to the claims to correct said minor informalities.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13 remain rejected under 35 USC § 112, first paragraph, regarding lack of enablement for a pharmaceutical composition for prophylaxis of all possible diseases, and treatment of all possible diseases other than hepatitis C (HCV) infection, as set forth on pages 3-5 of the prior office action mailed on 10/30/2006.

In the response received on 3/5/2007, the Applicants amended claims 11-13 to delete the phrase "for the treatment or prophylaxis of viral or immunomodulatory diseases". The Applicants argue that the currently amended claims do not read on treatment of all possible immunomodulatory diseases, or prophylaxis of viral or immunomodulatory diseases, and therefore the rejection is obviated.

These arguments have been fully considered and are not persuasive. As currently amended, the claims now recite a pharmaceutical composition comprising a "pharmacologically effective amount" of an isolated positional isomer of pegylated interferon alpha 2a. The claims do not recite any disease or condition for which the amount of pegylated interferon alpha 2a would be pharmacologically effective. Thus, the breadth of amended claim 11 is excessive because it reads on an amount of pegylated interferon alpha 2a that is pharmacologically effective for all possible diseases or conditions. As set forth in the previous office action, it is known that interferon alpha 2a can be used to treat HCV infection, and one of ordinary skill in the art would know how to prepare a pharmaceutical composition comprising an amount of pegylated interferon alpha 2a that is pharmacologically effective for the treatment of HCV. However, the skilled artisan would not be able to predict a pharmacologically effective amount of interferon alpha 2a for all possible diseases, and such a prediction would require further, undue experimentation.

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Furthermore, the claims read on positional isomers comprised of a PEG moiety with an average weight of 26,000 to 66,000 daltons. The specification does not provide guidance or examples showing that positional isomers comprised of PEG moieties of every possible molecular weight between 26,000 – 66,000 daltons would have the same biological properties and thus be effective in treating all possible diseases or conditions. Thus, one of ordinary skill in the art would require further, undue experimentation in order to create a composition for the treatment of all possible diseases or conditions wherein said composition comprises positional isomers of pegylated IFN- α with a PEG moiety of all possible molecular weights between 26,000 and 66,000 daltons.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejections withdrawn

Rejection of claims 11-13 under 35 USC § 112, second paragraph, as being indefinite regarding the phrase “immunomodulatory”, as set forth on pages 5-6 of the prior office action mailed on 10/30/2006, is withdrawn in response to Applicants’ amendments to the claims to delete the term “immunomodulatory” from the claims.

Rejections necessitated by amendment

Claims 11-13 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite a pharmaceutical composition comprising a “pharmacologically effective amount” of an isolated positional isomer of pegylated interferon alpha 2a. However, the claims do not recite any disease or condition for which the composition would be “pharmacologically effective”. Thus, it is not clear what doses would be “pharmacologically effective”.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejections withdrawn

1. Rejection of claims 1-3 and 11-13 under 35 USC § 102(b) as being anticipated by Monkarsh *et al*, as set forth on page 7 of the office action mailed on 10/30/2006, is withdrawn in response to Applicants amendments to the claims to recite an pegylated isomers of interferon alpha 2a wherein the average molecular weight of the polyethylene glycol (PEG) moiety is from 26,000 to 66,000 daltons, and Applicants' arguments that Monkarsh *et al* only teaches pegylated isomers of interferon alpha 2a wherein the PEG moiety is 5000 daltons.

2. Rejection of claims 1-3 and 11-13 under 35 USC § 102(b) as being anticipated by Gilbert *et al*, as set forth on page 7 of the office action mailed on 10/30/2006, is withdrawn in response to Applicants amendments to the claims to recite an pegylated isomers of interferon alpha 2a wherein the average molecular weight of the polyethylene glycol (PEG) moiety is from 26,000 to 66,000 daltons. The Applicants argue that Gilbert *et al* does not teach isolated positional isomers of pegylated interferon alpha 2a. Although Gilbert *et al* does in fact teach isolation of various isomers via cation exchange chromatography (see Exmaple 13), it is noted that Gilbert *et al* teaches pegylated isomers of interferon alpha 2a wherein the PEG moiety is either 5,000 or 12,000 daltons. For this reason, the rejection is withdrawn.

Rejections maintained

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3. Claims 1-6 and 11-13 remain rejected under 35 USC § 102(b) as being anticipated by Bailon *et al*, as set forth on pages 6-7 of the office action mailed on 10/30/2006. In the response received on 3/5/2007, the Applicants argue that Bailon *et al* does not meet the limitations of the claims as currently amended, because Bailon *et al* does not teach *isolated* positional positional isomers of pegylated interferon alpha 2a.

These arguments have been fully considered and are not persuasive. As set forth in the office action mailed on 10/30/2006, Bailon *et al* teaches positional isomers of interferon alpha 2a monopegylated on Lys31 and Lys134, wherein the PEG moiety is 40,000 daltons. These positional isomers would be expected, in the absence of evidence to the contrary, to have the same chemical structure and characteristics regardless of whether they are isolated or not, and therefore the claimed positional isomers of pegylated interferon alpha 2a of the instant application are not distinct from those disclosed in Bailon *et al*. Furthermore, the claims do not define or specify any degree of isolation (i.e. purity), and thus a composition or formulation comprising a pegylated IFN- α isomer of any purity could be considered an "isolated" positional IFN- α isomer. Therefore the pegylated IFN- α isomers of Bailon *et al* could be considered to be isolated isomers of IFN- α .

4. Claims 1-6 and 11-13 remain rejected under 35 USC § 102(b) as being anticipated by Barker *et al*, as set forth on page 8 of the office action mailed on 10/30/2006. In the response received on 3/5/2007, the Applicants argue that Barker *et al* does not meet the limitations of the claims as currently amended, because Barker *et al* does not teach *isolated* positional positional isomers of pegylated interferon alpha 2a.

These arguments have been fully considered and are not persuasive. As set forth in the office action mailed on 10/30/2006, Barker *et al* teaches positional isomers of interferon alpha 2a monopegylated on Lys31 and Lys134, wherein the PEG moiety is 40,000 daltons. These positional isomers would be expected, in the absence of evidence to the contrary, to have the same chemical structure and characteristics regardless of whether they are isolated or not, and therefore the claimed positional isomers of pegylated interferon alpha 2a of the instant application are not distinct from those disclosed in Barker *et al*. Furthermore, the claims do not define or specify any degree of isolation (i.e. purity), and thus a composition or formulation comprising a pegylated IFN- α isomer of any purity could be considered an "isolated" positional

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IFN- α isomer. Therefore the pegylated IFN- α isomers of Barker *et al* could be considered to be isolated isomers of IFN- α .

Claim Rejections - 35 USC § 103 – rejection necessitated by amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-6 and 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bailon *et al* in view of Monkarsh *et al*. The claims of the instant invention are drawn to isolated positional isomers of pegylated interferon alpha 2a, wherein said interferon alpha 2a is pegylated on Lys31 or Lys134, and wherein the PEG moiety is between 26,000 and 66,000 daltons, and specifically 40,000 daltons. The claims also recite a pharmaceutical composition comprising an isolated positional isomer of pegylated interferon alpha 2a.

As set forth *supra*, Bailon *et al* teaches positional isomers of pegylated interferon alpha 2a, wherein said interferon alpha 2a is pegylated on Lys31 or Lys134, and wherein the PEG moiety is 40,000 daltons.

Monkarsh *et al* teaches positional isomers of pegylated interferon alpha 2a, wherein said interferon alpha 2a is pegylated on Lys31 or Lys134, and also teaches methods of separating positional isomers of pegylated interferon alpha 2a (page 435, 1st column 3rd paragraph, page 436, 1st column 2nd paragraph – p. 437, 1st column, 1st paragraph), and specifically teaches isolation of Lys31 pegylated interferon alpha 2a, and Lys134 pegylated interferon alpha 2a (see p. 438, 2nd column, 1st paragraph and Table 1). Monkarsh *et al* also teaches determination of biological activity of each isomer (p. 438, 2nd column, last paragraph – p. 440, 1st column, 1st paragraph, and see Table 2).

As set forth *supra*, Bailon *et al* is deemed to meet the limitations of the instant claims by itself. However, even if this were not the case, the claims of the instant invention would still be obvious in view of the combination of Bailon *et al* and Monkarsh *et al*. A person of ordinary skill in the art would have the motivation to combine the teachings of Bailon *et al* and Monkarsh *et al* because both teach pegylation of interferon alpha 2a on Lys 31 and Lys134, and Monkarsh *et al*

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teaches specific methods for isolating these isomers and characterizing biological activity. Thus, it would be obvious to one of ordinary skill in the art to use the isolation methods of Monkarsh *et al* to isolate specific Lys31 and Lys134 isomers of pegylated interferon taught by Bailon *et al*. Furthermore, because specific conditions for pegylation are taught by both disclosures, and Monkarsh *et al* recites specific methods for isolation, one of ordinary skill in the art would also have a reasonable expectation of success in isolating positional isomers of pegylated interferon alpha 2a, wherein said interferon is pegylated on Lys31 or Lys134, and wherein the PEG moiety is 40,000 daltons.

Conclusion

No claim is allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

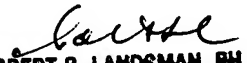
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
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ROBERT S. LANDSMAN, PH.D.
PRIMARY EXAMINER